2024-2274, 2024-2277, 2024-2278

United States Court of Appeals for the Federal Circuit

JAZZ PHARMACEUTICALS, INC.,

Plaintiff-Appellee,

– v. –

AVADEL CNS PHARMACEUTICALS, LLC,

Defendant-Appellant.

(For Continuation of Caption See Inside Cover)

On Appeals from the United States District Court for the District of Delaware in Nos. 1:21-cv-00691-GBW, 1:21-cv-01138-GBW, 1:21-cv-01594-GBW, Honorable Judge Gregory Brian Williams

NON-CONFIDENTIAL ANSWERING BRIEF OF PLAINTIFFS-APPELLEES JAZZ PHARMACEUTICALS, INC. AND JAZZ PHARMACEUTICALS IRELAND LIMITED

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JAZZ PHARMACEUTICALS, INC.,
JAZZ PHARMACEUTICALS IRELAND LIMITED,

Plaintiffs-Appellees,

– v. –

AVADEL CNS PHARMACEUTICALS, LLC,

Defendant-Appellant.

JAZZ PHARMACEUTICALS, INC.,
JAZZ PHARMACEUTICALS IRELAND LIMITED,

Plaintiffs-Appellees,

– v. –

AVADEL CNS PHARMACEUTICALS, LLC,

Defendant-Appellant.

Claims 14 and 24 of U.S. Patent No. 11,147,782 (Appx119) recite:

> **14.** A unit dose comprising a formulation of gamma-hydroxybutyrate,
>
> wherein the formulation comprises:
>
> a plurality of immediate release particles comprising gamma-hydroxybutyrate;
>
> a plurality of modified release particles comprising
>
> gamma-hydroxybutyrate;
>
> a viscosity enhancing agent; and
>
> an acid;
>
> wherein the viscosity enhancing agent and the acid are separate from the immediate release particles and the modified release particles.
>
> ***
>
> **24.** The unit dose of claim 14, wherein the unit dose is a sachet.

CERTIFICATE OF INTEREST

Case Number: 24-2274, 24-2277, 24-2278

Short Case Caption: *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*

Filing Party/Entity: Jazz Pharmaceuticals, Inc.
Jazz Pharmaceuticals Ireland Limited
Plaintiffs-Appellees

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

November 7, 2024 Signature: *s/ F. Dominic Cerrito*

Name: F. Dominic Cerrito

1. **Represented Entities.** Provide the full names of all entities represented by undersigned counsel in this case. Fed. Cir. R. 47.4(a)(1).

   Jazz Pharmaceuticals, Inc.
   Jazz Pharmaceuticals Ireland Limited

2. **Real Party in Interest.** Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. Fed. Cir. R. 47.4(a)(2).

   None.

3. **Parent Corporations and Stockholders.** Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. Fed. Cir. R. 47.4(a)(3).

   Jazz Pharmaceuticals plc.

4. **Legal Representatives.** List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

Quinn Emanuel Urquhart & Sullivan, LLP: Shira Bergman, Andrew S. Chalson, Abigail DeMasi, Elizabeth M. Devaney, Brian J. Forsatz, Alexandra Kim, Nicholas LoCastro, Catherine T. Mattes, Elizabeth J. Murphy, Raymond N. Nimrod, Christopher D. Porter, Shannon Prince, Krista M. Rycroft, Evangeline Shih, Eric C. Stops

Morris, Nichols, Arsht & Tunnell LLP: Jack B. Blumenfeld, Jeremy A. Tigan

5. **Related Cases.** Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

Yes.

If yes, concurrently file a separate Notice of Related Case Information that complies with Fed. Cir. R. 47.5(b). **Please do not duplicate information.** This separate Notice must only be filed with the first Certificate of Interest or, subsequently, if information changes during the pendency of the appeal. Fed. Cir. R. 47.5(b).

6. **Organizational Victims and Bankruptcy Cases.** Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

Not applicable.

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Pursuant to Federal Circuit Rule 25.1(e)(1)(B), Plaintiffs-Appellees provide the following description of the general nature of the material redacted in the nonconfidential version of its Answering Brief:

The material omitted on pages 16, 49, and 60 of this Answering Brief relate to the confidential business information subject to a protective order.

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STATEMENT OF RELATED CASES

These consolidated appeals arise from three combined proceedings in the U.S. District Court for the District of Delaware: *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*, No. 1:21-cv-00691-GBW (D. Del.); *Jazz Pharmaceuticals, Inc., et al. v. Avadel CNS Pharmaceuticals*, LLC, No. 1:21-cv-01138-GBW (D. Del.); and *Jazz Pharmaceuticals, Inc., et al. v. Avadel CNS Pharmaceuticals, LLC*, No. 1:21-cv-01594-GBW (D. Del.). This Court previously decided an appeal arising from one of those actions: *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*, No. 23-1186, 60 F.4th 1373 (Lourie, J, joined by Reyna and Taranto, JJ.) (Fed. Cir. 2023) (appeal from D. Del. No. 1:21-cv-00691-GBW).

The following actions may affect or be affected by this Court's decision in the present appeal: *Avadel CNS Pharmaceuticals, LLC, et al. v. Jazz Pharmaceuticals, Inc., et al.*, No. 1:22-cv-00487-GBW (D. Del.) (filed Apr. 14, 2022); *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*, No. 1:22- cv-00941-GBW (D. Del.) (filed July 15, 2022); and *Jazz Pharmaceuticals, Inc. v. Becerra*, No. 1:23-cv-01819-APM (D.D.C.) (filed June 22, 2023).

PRELIMINARY STATEMENT

Appellant Avadel CNS Pharmaceutical LLC's assertion that the safe harbor defense requires this Court to vacate or modify the permanent injunction on appeal cannot succeed because Avadel failed to plead this affirmative defense, never raised it in the briefing on the permanent injunction, failed to offer any evidence to support it in the district court, and unconditionally stipulated to infringement. This Court should affirm.

This appeal concerns a limited permanent injunction that the U.S. District Court for the District of Delaware (Williams, J.) entered following a jury trial. Prior to trial, Avadel stipulated that its product, Lumryz, infringes the patent of Appellees Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited ("Jazz")—a patent that protects an innovative dosage form that improves the administrability of modified-release oxybate through the use of an acid and a viscosity-enhancing agent in a sachet. After the jury rejected Avadel's invalidity defenses, Jazz sought a permanent injunction. The district court issued an injunction that balanced the fact that patients already were taking Avadel's infringing product for the treatment of narcolepsy with the

harm to Jazz that would result from Avadel expanding its infringement beyond narcolepsy, including to the treatment of another sleep disorder—idiopathic hypersomnia ("IH").

At no point from the filing of the initial complaint seeking injunctive relief in 2021 through trial and then post-trial briefing on the permanent injunction did Avadel raise the argument that Avadel now asserts entitles it to relief from this Court—that the safe harbor in 35 U.S.C. § 271(e)(1) barred the district court from enjoining future clinical trials, an open-label extension ("OLE"), or a request for FDA approval of new indications. And, although the application of the safe harbor defense is question of fact, Avadel never presented evidence to the district court to support any finding that the safe harbor applies.

Such circumstances bar Avadel's argument that the district court abused its discretion in enjoining Avadel from expanding the making, using, and offering for sale of Lumryz beyond the treatment of narcolepsy. At the threshold, the safe harbor set forth in Section 271(e)(1) of the Patent Act is an affirmative defense that Avadel never pled. While Avadel now contends that Jazz carved out safe harbor-protected conduct from its complaint, that is not accurate. Rather, while

Jazz indicated it would not seek damages for Avadel's past conduct in getting Lumryz approved to the extent the safe harbor applied to such conduct, Jazz's complaint never suggested that Avadel could show the safe harbor applied to conduct undertaken after it had been adjudicated an infringer and received approval for Lumryz. And under no reading of the complaint did Jazz relieve Avadel of the burden of *proving* that any such conduct fell within the safe harbor. Without question, Avadel's failure to plead the defense prejudiced Jazz: the entirety of discovery, litigation strategies, evidentiary presentations at trial, and briefing on the permanent injunction all took place without Jazz ever knowing that Avadel belatedly would raise the specter of the safe harbor. The law precludes Avadel from raising the defense now.

Even if this Court looks beyond this fundamental defect in Avadel's arguments on appeal, Avadel cannot show any abuse of discretion in the district court's decision to enjoin future clinical trials, the OLE, or a request for FDA approval for IH. Although Avadel contends that the safe harbor defense applies to certain enjoined conduct, Avadel did not raise the safe harbor in its briefing on the injunction. The district court cannot have abused its discretion in declining to adopt an argument not made.

Separately, the safe harbor defense does not apply automatically as a matter of law upon Avadel's say-so, but instead requires evidence proving the challenged conduct falls within the scope of the safe harbor. Yet Avadel failed to present evidence in the district court supporting such a factual finding and cannot do so for the first time on appeal. Indeed, because Avadel did not raise this argument, Jazz never had the opportunity to put its own contrary evidence into the record. Were this Court to consider the merits of Avadel's safe harbor arguments, the record shows that Avadel has not proven that the safe harbor covers future clinical trials, the OLE, or a request that the FDA approve IH.

Nor can Avadel prevail on its other newly raised defenses. Neither Section 271(a) of the Patent Act nor the First Amendment provides a license for Avadel to trample Jazz's legally recognized patent rights. And, even if Avadel could prove non-infringement under these theories, this Court has made clear that district courts may narrowly enjoin non-infringing conduct as necessary to prevent infringing conduct.

Finally, Avadel has not demonstrated any abuse of discretion as to the *eBay* factors. The district court tailored a limited injunction that allows narcolepsy patients to continue receiving Avadel's infringing

product but prevents Avadel from expanding to other indications. Avadel specifically sought to "switch" patients from Jazz's products to Avadel's infringing product, irreparably harming Jazz, and the other *eBay* factors all supported entry of the injunction.

This Court should affirm.

COUNTERSTATEMENT OF ISSUES

1. Whether the district court properly enjoined conduct that an adjudicated infringer asserts on appeal fell within the safe harbor when the infringer failed to plead the safe harbor affirmative defense in its answer or raise the defense in the injunction briefing, failed to present evidence in the district court in support of its application, and unconditionally stipulated to infringement before trial.

2. Whether the district court properly exercised its discretion in issuing an injunction against further infringing conduct based on factual findings that infringement would irreparably harm the patentee and the patentee did not have an adequate remedy at law, that the balance of hardships favored an injunction, and that the public interest favored an injunction.

COUNTERSTATEMENT OF THE CASE

A. Constitutional And Statutory Framework

The "right to maintain exclusivity" is "a hallmark and crucial guarantee of patent rights" that the framers enshrined in the Constitution. *Apple Inc. v. Samsung Elecs. Co.*, 809 F.3d 633, 642 (Fed. Cir. 2015); U.S. Const. Art. I, § 8, cl. 8 (referring to inventors' "exclusive Right to their respective . . . Discoveries").

Congress has consistently protected patent rights through legislation. For example, Congress has broadly empowered courts with the authority to grant injunctions to prevent infringement. *See* 35 U.S.C. § 283; *see also Apple*, 809 F.3d at 647 (explaining injunctions are "vital" to reinforcing "the importance of the patent system in encouraging innovation"). Courts have broadly construed the definition of infringement, *see, e.g.*, *Centillion Data Sys., LLC v. Qwest Commc'n Int'l, Inc.*, 631 F.3d 1279, 1283-84 (Fed. Cir. 2011) ("[C]ourts have interpreted the term 'use' broadly[.]"), and "historically . . . have 'granted injunctive relief upon a finding of infringement in the vast majority of patent cases,'" *Apple*, 809 F.3d at 638-39 (quoting *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388, 395 (2006)).

Congress declared that, "[e]xcept as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent." 35 U.S.C. § 271(a). Congress provided one narrow safe harbor exception to this provision—section 271(e)(1)—an affirmative defense that applies in limited circumstances to conduct that otherwise would constitute infringing activity. *See Edwards Lifesciences Corp. v. Meril Life Scis. Pvt. Ltd.*, 96 F.4th 1347, 1351 (Fed. Cir. 2024).

Section 271(e)(1) protects only certain conduct related to "a patented invention" that is "solely for uses reasonably related to the development and submission of information" to the FDA. *See* 35 U.S.C. § 271(e)(1). In other words, "for each act of infringement the safe harbor is available only for acts or uses that bear a reasonable relation to the development and submission of information to the FDA." *Edwards*, 96 F.4th at 1353.

Congress codified the safe harbor exception to prevent *de facto* patent life extensions as a result of the FDA premarket approval process. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 670-71 (1990). No

such *de facto* patent life extension exists when the FDA has approved a competitor's infringing product and the competitor is already commercially marketing that infringing product *before* the expiration of the patentee's patent. Indeed, "[t]he legislative history makes clear that the exemption 'does not permit the commercial sale of a patented drug by the party using the drug to develop [federal regulatory] information.'" *Edwards*, 96 F.4th at 1358 (Lourie, J., dissenting) (quoting H.R. Rep. No. 98-857, pt. 1, at 45). Consistent with that intent, this Court has never extended the safe harbor to permit an already-adjudicated infringer to expand its commercial marketing beyond one therapeutic indication to another.

B. Factual Background

1. Jazz's Oxybate Products

Jazz develops and markets treatments for serious diseases with limited or no therapeutic options. One primary area of focus is sleep disorders, including the treatment of narcolepsy and IH. Appx9254-9255, 484:16-485:3; Appx11603.

Jazz entered the sleep space in 2005 when it acquired Orphan Medical and its sodium oxybate product, Xyrem®. Appx5272, ¶11. Since 2005, Xyrem has been approved for the treatment of cataplexy and

excessive daytime sleepiness ("EDS") in adult patients with narcolepsy. Appx5272, ¶11. In 2018, based on Jazz's clinical studies, the FDA expanded Xyrem's approval to patients 7 years of age or older, and Xyrem became the first drug approved for pediatric narcolepsy patients. Appx5272, ¶11; Appx9154, 89:15-24.

Jazz established Xyrem as a market-leading treatment for narcolepsy. Appx5273, ¶12. Jazz, however, saw potential areas for improvement. Xyrem is a high-sodium product that is dosed twice nightly. Therefore, in 2009, Jazz explored a formulation that could reduce the high amount of sodium consumed with a daily Xyrem treatment. Appx5273, ¶13. Narcolepsy is a lifelong disorder requiring long-term treatment and associated with cardiovascular comorbidities. Appx9155, 90:9-91:17. Increased sodium intake increases the likelihood of cardiovascular disease. Appx5711. Jazz saw this improvement as critical to patient safety. Appx9155, 93:18-24.

Jazz also explored formulations that could be administered once-nightly to improve patient convenience. But, in 2009 and 2010, Jazz was a small company on the verge of closing its doors. Appx9153, 82:9-19. It did not have the bandwidth to fully tackle both potential improvements

at once. Appx9155-9156, 93:14-94:8; *see also* Appx9171-9172, 157:8-158:2. Jazz decided to first focus on reducing the sodium burden of Xyrem while providing an oxybate product with similar efficacy. Appx9155-9156, 93:14-94:8; *see also* Appx9171-9172, 157:8-158:2.

Jazz invested approximately 10 years and substantial financial resources into developing a new oxybate formulation with a greatly reduced chronic sodium burden and ushering it through FDA approval. Appx5273, ¶13. In July 2020, Jazz's low sodium oxybate, Xywav, was approved for the treatment of cataplexy and EDS in narcolepsy. Appx5273, ¶14.

The FDA awarded Xywav orphan drug exclusivity as being clinically superior to the only sodium oxybate treatment on the market, Xyrem, due to its greatly reduced chronic sodium burden. Appx5274, ¶16.

Through Jazz's additional investment in clinical trials, Xywav also became (and remains) the first and only FDA approved drug for the treatment of IH. Appx5273-5274, ¶15. IH is a rare and chronic sleep disorder, distinct from narcolepsy, that causes EDS even after a full night of sleep. Appx6461-6464, ¶¶13-18. Approximately 45,000 patients have

been diagnosed with IH. Appx5273-5274, ¶15. And while Xywav, like Xyrem, is approved to be dosed twice nightly with respect to treating narcolepsy symptoms (Appx9155, 91:18-19), Xywav is FDA-approved and equally effective in treating IH with only once-nightly dosing. Appx6464-6466, ¶¶19-25; Appx6563; Appx6606-6617.

Xywav is the core of Jazz's sleep brand and the most valuable of Jazz's oxybate products, which together grossed $1.84 billion in 2023 (48% of Jazz's total revenue). Appx4717. Since its November 2020 launch, Xywav sales have increased rapidly: $15 million in 2020, $535 million in 2021, $958 million in 2022 (Appx4715), and $1.272 billion in 2023 (Appx4717). And the number of patients taking Xywav for IH also has increased dramatically year-over-year—leaping 59% from 2022 to 2023. Appx4717; Appx9017, 17:12-14.

2. Jazz's Invention Of Claim 24 Of The '782 Patent

Jazz also has worked toward the development of a once-nightly oxybate dosage form for patient convenience. In 2015, Jazz began focusing on improving the administrability of certain formulations by introducing ingredients to make the dosage forms safe and easier for

patients to ingest. Appx9171, 155:18-156:5. The invention in claim 24 of the '782 patent resulted from this work.

Claim 24 of the '782 patent is a product claim. It is not a method claim. The invention is a unit dose sachet comprising a formulation of immediate release and modified release particles comprising gamma-hydroxybutyrate (oxybate) with a viscosity enhancing agent and acid separate from the particles. Appx119; *see also* No. 21-691, ECF 688 ¶12. To arrive at the invention, the inventors conceived of three solutions to potential administrability issues arising for multi-particulate oxybate formulations with a mix of immediate release and modified release particles. Appx9171, 155:18-156:5.

First, the inventors realized that, when the particles are suspended in water, they can sink to the bottom of the glass and remain there, resulting in the patient not receiving the full dose. Appx9171, 155:18-156:5. They solved this problem using a viscosity enhancing agent separate from the particles in the sachet that would thicken the suspension and prevent the particles from immediately sinking to the bottom of the glass. Appx9171, 156:10-17; No. 21-691, ECF 688 ¶¶14-15.

Second, the inventors realized that, when these particles were mixed with water prior to ingestion by the patient, the modified release particles would dissolve and release their oxybate if the pH was not acidic enough. Appx9171, 155:18-156:5. The result would be a patient receiving a potentially dangerous level of oxybate in the bloodstream. Appx9171, 155:18-156:5. The inventors discovered they could include an acid separate from the particles that would prevent the modified release particles from dissolving early. Appx9171, 156:18-157:2; Appx9173, 164:15-166:8; No. 21-691, ECF 688 ¶13.

Third, the inventors needed to determine the right dosage form to present the formulation to the patient. Appx9171, 155:18-156:3. They determined that maintaining the formulation in a sachet could solve that problem. Appx9171, 156:6-9.

3. Avadel's Infringing Product And Commercialization Strategy

Before 2020, Avadel was a multi-product company that primarily marketed hospital injectable medicines. Appx2257. Only in 2020 did Avadel decide to divest all its products to focus solely on developing Lumryz to treat narcolepsy. Appx9253, 479:1-7.

Avadel's now-only product, Lumryz, is a multi-particulate extended release sodium oxybate formulation indicated for the treatment of cataplexy and EDS in narcolepsy. Avadel admits that Lumryz infringes claim 24 of the '782 patent. Appx4311-4313.

In December 2020, Avadel submitted an NDA pursuant to 21 U.S.C. § 505(b)(2) requesting approval of what would be called Lumryz. Appx9255, 488:4-7. The Lumryz NDA relied in part on the FDA's finding of safety and efficacy for Xyrem. Appx9255-9256, 487:24-489:22. As such, Avadel did not run certain clinical trials for approval of its sodium oxybate product because it relied on clinical data generated by Jazz and its predecessor Orphan Medical. Appx9255-9256, 488:23-489:19. Avadel also relied on Jazz's clinical trials in pediatric narcolepsy to support its pediatric narcolepsy indication request. Appx7624-7629; Appx7630-7635. As a result, Avadel was recently granted approval for pediatric narcolepsy without conducting any clinical trials. *See* Avadel October 17, 2024 Press Release (available at https://investors.avadel.com/news-releases/news-release-details/avadel-pharmaceuticals-announces-fda-approval-lumryztm-sodium).

On May 1, 2023, the FDA approved Lumryz for use once-at-bedtime for the treatment of cataplexy and EDS in narcolepsy. Appx9249, 463:8-10. Avadel commercially launched Lumryz in June 2023 (Appx9257, 495:10-12)—as this litigation was pending—with full knowledge it may infringe a valid Jazz patent.

While the active ingredient in Lumryz is the same as Xyrem and thus has the same sodium load as Xyrem, (Appx9256, 491:5-7), the FDA granted Lumryz orphan drug exclusivity based on its finding that Lumryz was clinically superior to Jazz's oxybate products in narcolepsy, deeming once-nightly dosing a "major contribution to patient care." Appx9256-9257, 492:21-493:9. The FDA never determined that Lumryz had greater safety or efficacy than Jazz's products. Appx9256, 491:8-492:5. Quite the opposite, the FDA found that Xywav's significantly lower amount of sodium is "safer" for "all patients with narcolepsy." Appx11108-11109.

Avadel's primary commercial strategy has been and continues to be to switch patients from Jazz's oxybate products to Lumryz. Appx9264-9265, 524:21-22; *see also* Appx11402. As Avadel stated, "the majority of patients [on Lumryz] are switch patients with more coming from the

[Xywav] mixed salt." Appx4609, 10:1-12:19; Appx4624, 10:1-15; *see also* Appx5277, ¶¶ 25-26.

As part of its direct competition with Jazz, Avadel has aimed to negotiate insurance coverage for Lumryz, seeking and obtaining preferred status with various pharmacy benefit managers ("PBMs") (*see* Appx11614), through increased rebates back to the PBMs. Jazz and Avadel make revenue by gaining reimbursement from insurance companies. Appx9267, 534:4-8; Appx5278-5279, ¶¶ 27-29. Insurance companies contract with PBMs to negotiate prices for patients covered by an insurance plan. The PBMs, in turn, negotiate with drug companies for rebates.[1] Appx5278-5279, ¶¶ 28-29. In negotiations with insurance companies, Avadel has attempted to COMMERCIALLY SENSITIVE INFORMATION [redacted]. Appx4567-4568. These tactics have caused Jazz to [redacted] for Xywav to insurance companies to [redacted], which erodes its price. Appx4567-4568.

Avadel does not dispute that it stands to make billions of dollars on infringing sales of Lumryz to treat narcolepsy, which the district court

[1] Despite Avadel's mudslinging concerning the price of Jazz's products (Avadel's Confidential Opening Brief, ECF No. 28 ("Br.") at 8), Avadel has priced Lumryz at parity with Xywav. Appx9261, 509:23-510:15.

did not enjoin. *See* Appx4579-4580; Appx6066; Appx7553. Regardless, Avadel now seeks to add an indication for IH to Lumryz's label. Appx9263, 519:14-16. Avadel views the new IH market as holding "a lot of opportunity" because "there's a robust patient population . . . with only one currently FDA approved treatment, [Xywav]." Appx4612. Avadel already has "seen claims and requests coming in for off label uses of LUMRYZ [for IH]," and has sold its product off-label for IH before the injunction. Appx4626.

But, unlike the narcolepsy market, Xywav has approval for once-nightly treatment of IH, as the district court recognized. Appx30. Avadel launched a clinical trial for IH (the "IH Trial") on July 31, 2024 (after telling the district court it would not do so if enjoined), slightly before the district court issued the injunction order. ECF 7, Ex. D. Avadel's IH Trial does not compare Lumryz and Xywav. Instead, it is a placebo-controlled study of the safety and efficacy of Lumryz in subjects with IH. The results of this trial thus cannot reveal whether "Lumryz is more effective than Xywav," Br. 19-20, in treating IH.

C. Procedural Background

Jazz sued Avadel for infringement of the '782 patent on November 10, 2021. Appx10157-10360. In its complaint, and consistently thereafter, Jazz has sought to enjoin all infringing activity. Appx10169-10170. At all times, both before and after Avadel launched Lumryz, Jazz sought "[a] permanent injunction enjoining Avadel and its officers, agents, attorneys and employees, and those acting in privity and/or concert with them, from making, using, selling, offering to sell, and/or importing Avadel's Proposed Product until after the expiration of the patent-in-suit, or any later expiration of exclusivity to which Plaintiffs are or become entitled" with no caveats or carveouts. Appx10008 (June 2023 amended complaint); *see also* Appx10169 (original complaint requesting same).

In its complaint, Jazz acknowledged that some of Avadel's actions in gaining approval of Lumryz may have been non-infringing under the 35 U.S.C. § 271(e)(1) safe harbor and exempted such actions from its request for *past* infringement damages. *See* Appx10008 ("To the extent that Avadel has committed any acts with respect to the formulations claimed in the patent-in-suit, other than those acts expressly exempted

by 35 U.S.C. § 271(e)(1), that Plaintiffs *be awarded damages for such acts*." (emphasis added)); *see also* Appx10169. But Jazz deliberately excluded any similar carveout from its request for injunctive relief, which focused on Avadel's *future* conduct. Appx10008. Even though Jazz had flagged the possibility that the safe harbor potentially could apply to past infringement, Avadel's Answers never asserted as an affirmative defense that any conduct qualified as non-infringing under the safe harbor. *See* Appx10378-10381; Appx10422-10425.

Before trial in February 2024, Avadel unconditionally stipulated to infringement of claim 24. Appx4311-4313. Avadel's stipulation made no reservation for any uses for which Avadel wished to present evidence of non-infringement, including those Avadel now claims are subject to the safe harbor. The stipulation so ordered by the district court read: "NOW THEREFORE, IT IS HEREBY STIPULATED AND AGREED by Jazz and Avadel that Avadel's manufacture, use, offers for sale, sales, and/or importation of Avadel's Lumryz™ drug product infringes claim 24 of the '782 patent pursuant to 35 U.S.C. § 271(a), to the extent claim 24 of the '782 patent is found not to be invalid or unenforceable." Appx4312.

Avadel pleaded numerous, non-safe-harbor affirmative defenses to infringement of the '782 patent (*see* Appx10378-10381; Appx10422-10425), but asserted and offered purported evidence on only three defenses at trial—invalidity for lack of written description, lack of enablement, and improper inventorship. Appx4375-4378. The jury rejected Avadel's defenses, and awarded Jazz damages in the form of a reasonable royalty for Avadel's past infringing sales. Appx4380-4391.

Following trial, Jazz sought an injunction under 35 U.S.C. § 283 prohibiting Avadel "from infringing in any way Claim 24 of the '782 patent, by making, using, or selling Lumryz or any product not more than colorably different from Lumryz, through and including the expiration date of the '782 patent" and requested that "Avadel may not seek approval from the U.S. Food and Drug Administration for any indication that was not already part of Lumryz's approved product labeling as of March 4, 2024." Appx4550. Jazz excluded certain specific Avadel infringing activities from its request, namely: making, using, and selling Lumryz (a) for patients prescribed Lumryz as of the effective date of the injunction; (b) in *currently-ongoing* clinical trials and studies; (c) to

update data in old studies if necessary; and (d) to re-run necessary tests for quality control for regulators or customers. Appx4550.

In briefing the injunction, consistent with its unconditional stipulation in the action and its failure to plead the safe harbor as an affirmative defense, Avadel did not raise any non-infringement defense to any of the conduct Jazz sought to enjoin. *See generally* Appx5652-5901. At the permanent injunction hearing, Avadel for the first time suggested the safe harbor may apply, but Jazz disagreed. Appx9100-9101. Prior to that, Avadel had never so much as hinted that it considered certain future uses non-infringing. At the same hearing, Avadel told the district court that it would not proceed with an IH clinical trial if enjoined (Appx9064, 64:15-21; Appx9086, 86:1-8), despite the fact that the protocols for its IH Trial and subsequent OLE had been finalized more than four months prior on January 31, 2024 (ECF 23, Stern Decl. Ex. 2).[2] Avadel made no non-infringement arguments under Section 271(a) or the First Amendment in its briefing or at the hearing.

[2] Avadel reneged on its representation. On July 31, 2024, while the injunction decision was pending, Avadel launched the IH Trial. Appx40.

On August 27, 2024, the district court enjoined Avadel from "seeking approval from the [FDA] and marketing Lumryz for the treatment of IH" "or for any indication that was not already part of Lumryz's approved product labeling as of March 4, 2024" and "from infringing in any way Claim 24 of the '782 patent, by making, using, or selling Lumryz or any product not more than colorably different from Lumryz, through and including the expiration date of the '782 patent." Appx36-37. The district court enjoined all uses of Lumryz except for the specific carveouts of making, using, and selling Lumryz: (a) for the treatment of narcolepsy; (b) for the patients who were prescribed Lumryz as of the effective date of the injunction conditional on Avadel paying appropriate remuneration; (c) in currently-ongoing clinical trials and studies as of August 27, 2024; (d) to update data in old studies if necessary; and (e) to re-run necessary tests for quality control for regulators or customers. Appx36-37; Appx40-41.

Avadel requested an emergency stay of the injunction at the district court on September 3, 2024. Appx7485-7492. While the district court considered the stay motion, the parties briefed Avadel's emergency stay request before this Court. The district court issued an order denying the

stay and clarified that Avadel may proceed with the IH Trial because it was a currently-ongoing clinical trial as of the date that the district court ordered the injunction. Appx40. The district court also clarified that, "while the Order enjoins Avadel from seeking FDA approval for IH, the Order does not enjoin Avadel from *submitting information or results* from ongoing clinical studies to the FDA." Appx41.

But the district court found that enjoining the OLE would not irreparably harm Avadel and did not stay the injunction with respect to the OLE. Appx43. As this Court explained, the district court stay order "clarified" the scope of the injunction and did not expand it. ECF 30 at 3. This Court then issued a stay only with respect to "initiating new clinical trials or studies" and denied the stay request in all other respects. Appx43.

SUMMARY OF ARGUMENT

The district court did not abuse its discretion in issuing a limited injunction prohibiting Avadel from conducting certain activities that infringe Jazz's patented invention.

I. Avadel's newly raised non-infringement arguments fail because Avadel failed to raise or prove the safe harbor defense in the

district court. To start, Avadel is foreclosed from raising the safe harbor because it failed to plead it as an affirmative defense, as required. The parties litigated the entire case—from discovery through trial through post-trial injunction briefing—without notice that Avadel would raise the safe harbor as a defense. Beyond that, Avadel unconditionally stipulated to infringement. Avadel failed to preserve the arguments it now raises and cannot use its belated invocation of the safe harbor to undo the district court's injunction or its unqualified stipulation of infringement.

Because Avadel never tried to prove that the safe harbor defense applies, the district court could not have abused its discretion or clearly erred in declining to find the requirements of the safe harbor defense met. Contrary to Avadel's insinuations, application of the safe harbor defense is a fact-intensive inquiry. Yet Avadel presented no factual support showing that the safe harbor defense applies to the conduct the district court enjoined. For instance, to prove the defense, Avadel had to offer factual evidence showing that its use of Jazz's patented invention is solely for uses reasonably related to the development and submission of information to the FDA and that the Lumryz dosage form falls under the safe harbor's "patented invention" requirement. Avadel presented no

such evidence or argument below and cannot do so for the first time on appeal.

Likewise waived are Avadel's arguments as to Section 271(a) of the Patent Act and the First Amendment—neither of which Avadel raised in the district court prior to issuance of the injunction. In any event, Section 271(a) provides no protection because Avadel is using Jazz's patented invention—even if one of the uses is to expand the FDA-approved indications of Lumryz. And the First Amendment does not license Avadel to undertake infringing conduct. At a minimum, the district court did not abuse its discretion because a district court may narrowly enjoin non-infringing conduct as necessary to prevent infringing conduct. Here, the district court was well within its discretion to narrowly enjoin Avadel from seeking FDA approval, conducting additional clinical trials, and conducting an OLE because doing so was necessary to prevent Avadel from infringing Jazz's patent by marketing the already-commercially-available Lumryz for IH.

II. Avadel also fails to show any abuse of discretion as to the remaining factors governing the issuance of a permanent injunction.

Avadel makes no argument that the district court clearly erred in finding, based on the record, that Avadel's entrance into the IH market with an infringing product would irreparably harm Jazz and leave Jazz with no adequate remedy at law. Unable to dispute the district court's findings, Avadel raises a new "causal nexus" argument. That argument is not preserved for appeal. Even were it preserved, a clear and direct connection exists between Avadel seeking FDA approval and the harm the injunction redresses because such action necessarily and inherently would result in marketing Lumryz for IH—an objective that Avadel concedes in its opening brief.

Nor has Avadel demonstrated that the district court abused its discretion in deciding that the balance of the equities favors an injunction. Unable to dispute the district court's findings, Avadel raises a new "patent term extension" argument. That argument is neither preserved for appeal nor meritorious. Avadel has admitted that it expects its current IH Trial to be sufficient to request FDA approval for IH. The district court's clarified injunction allows Avadel to submit information from the IH Trial to the FDA for its desired IH indication.

Avadel can then ask for FDA approval on the day Jazz's '782 patent expires. No alleged patent term extension concern exists here.

Finally, Avadel cannot show that the district court abused its discretion in deciding that the public interest favors an injunction. Yet again unable to dispute the district court's findings, Avadel essentially asks the Court to appoint the FDA as factfinder here. But the district court is the appropriate factfinder in the injunction context. Accepting Avadel's argument would elevate the FDA at the expense of the judiciary and would delay entry of a final judgment in this case, and those similarly situated, for years.

STANDARD OF REVIEW

This Court "review[s] the decision to grant a permanent injunction for an abuse of discretion." *SiOnyx LLC v. Hamamatsu Photonics K.K.*, 981 F.3d 1339, 1349 (Fed. Cir. 2020). A district court abuses its discretion when it "ma[kes] a clear error of judgment in weighing relevant factors or exercise[s] its discretion based upon an error of law or clearly erroneous factual findings." *Id.* This Court "review[s] the district court's conclusion as to each *eBay* factor for abuse of discretion and its underlying factual findings for clear error." *Apple*, 809 F.3d at 639. As

this Court has recognized, its task "is solely to review the district court's decision for an abuse of discretion," and not to "weigh evidence [itself] to reach a conclusion on injunctive relief," as that is the role of the first-line court of equity. *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 811 (Fed. Cir. 2007).

Infringement is a question of fact the Court reviews for clear error. *Natera, Inc. v. NeoGenomics Labs., Inc.*, 106 F.4th 1369, 1375 (Fed. Cir. 2024).

This Court applies regional circuit law to the issue of waiver of an affirmative defense. *Ultra-Prevision Mfg., Ltd. v. Ford Motor Co.*, 411 F.3d 1369, 1376 (Fed. Cir. 2005); *see also Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743, 756 (Fed. Cir. 2019). The Third Circuit deems an affirmative defense waived "if the party raising the defense did not do so at a 'pragmatically sufficient time' and if the opposing party would be prejudiced if the defense were allowed." *In re Frescati Shipping Co., Ltd.*, 886 F.3d 291, 313 (3d Cir. 2018).

ARGUMENT

I. THE DISTRICT COURT DID NOT ABUSE ITS DISCRETION IN ISSUING A LIMITED INJUNCTION PROHIBITING CERTAIN INFRINGING ACTIVITIES

Avadel's failure to raise the safe harbor as an affirmative defense, unconditional stipulation of infringement, and its failure to raise any such argument in its injunction briefing bar Avadel's attack on the injunction on appeal. Even if considered, application of the safe harbor is a fact-intensive inquiry for which Avadel cannot show any clear error in light of the dearth of record evidence in the district court. The Patent Act's prohibition on "use" of an infringing product applies to seeking FDA approval and the First Amendment does not protect infringing conduct. The district court did not abuse its discretion in enjoining Avadel's efforts to expand its infringing conduct.

A. Avadel Waived Its Safe Harbor Arguments

At the threshold, because Avadel repeatedly failed to argue any safe harbor defense and stipulated to infringement—without qualification—at trial, Avadel has not preserved such argument for appeal. Allowing Avadel to resurrect that waived defense now would unduly prejudice Jazz.

1. Avadel Failed To Plead A Safe Harbor Defense

"In responding to a pleading, a party must affirmatively state any avoidance or affirmative defense." Fed. R. Civ. P. 8(c). "Failure to raise an affirmative defense by responsive pleading or by appropriate motion generally results in the waiver of that defense." *Chainey v. Street*, 523 F.3d 200, 209 (3d Cir. 2008). "Waiver is appropriate if the party raising the defense did not do so at a 'pragmatically sufficient time' and if the opposing party would be prejudiced if the defense were allowed." *In re Frescati*, 886 F.3d at 313.

The safe harbor "is an affirmative defense." *Regenxbio Inc. v. Sarepta Therapeutics, Inc.*, No. 20-1226, 2022 WL 609141, at *2 (D. Del. Jan. 4, 2022); *see also Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d 1334, 1336-37 (Fed. Cir. 2007) (listing safe harbor exception as a "defense" presented by defendant); *Edwards*, 96 F.4th at 1355 (calling safe harbor a "defense"); *Amgen Inc. v. Hospira, Inc.*, 944 F.3d 1327, 1337 (Fed. Cir. 2019) (same). "Since it is an affirmative defense, Defendants must plead it in their answer" and "prove [it] by a preponderance of the evidence." *Immunomedics, Inc. v. Roger Williams Med. Ctr.*, No. 15-4526, 2017 WL 58580, at *9 (D.N.J. Jan. 4, 2017) (citing *Merck KGaA v. Integra*

Lifesciences I, Ltd., 545 U.S. 193, 200 (2005) and *Schmidt v. Skolas*, 770 F.3d 241, 249 (3d Cir. 2014)).

Avadel does not dispute that the safe harbor is an affirmative defense that it failed to plead or pursue. Br. 27. At a minimum, Avadel could have raised a safe harbor defense in its Answer to Jazz's amended complaint on July 10, 2023 (Appx10411-10455), which was *after* Avadel publicly stated in June 2023 that it planned to seek an IH indication (Appx11591). But Avadel did not do so. Instead, Avadel claims it "had no basis to raise [a safe harbor] affirmative defense" because "Jazz's amended complaint specifically disclaimed infringement as to any 'acts expressly exempted by 35 U.S.C. § 271(e)(1).'" Br. 27. Such an argument cannot be reconciled with Jazz's prayers for relief.

Jazz's second prayer expressly requests "[a] permanent injunction enjoining Avadel and its officers, agents, attorneys and employees, and those acting in privity and/or concert with them, from making, using, selling, offering to sell, and/or importing Avadel's Proposed Product until after the expiration of the patent-in-suit, or any later expiration of exclusivity to which Plaintiffs are or become entitled." Appx10008; *see also* Appx10169 (original complaint requesting same). Jazz requested a

permanent injunction prohibiting all future infringing activity with no exemption for any future conduct. Appx4545-4550. As such, Avadel has known that Jazz sought to enjoin *all* future infringing activity since the inception of this action. Appx10008; Appx10169; Appx4545-4550.

In arguing otherwise, Avadel references (Br. 27) Jazz's fourth prayer for relief, which states: "To the extent Avadel *has committed* any acts with respect to the formulations claimed in the patent-in-suit, other than those acts expressly exempted by 35 U.S.C. § 271(e)(1), that Plaintiffs be awarded *damages* for such acts." Appx10008 (emphasis added). This limited reference to the safe harbor relates only to *past infringement damages*, such as Avadel's initial clinical studies *before* Lumryz's approval. And, in any event, nowhere does Jazz's complaint relieve Avadel of the obligation to plead and prove the defense for any disputes about whether certain conduct falls within the scope of the safe harbor. *Immunomedics, Inc.*, 2017 WL 58580, at *9 (defendant must plead and prove affirmative defense).

If Avadel believed any of its *future* acts were subject to the safe harbor, it was incumbent upon Avadel to plead that. Yet Avadel answered both complaints, never asserted the safe harbor affirmative

defense, and never sought to amend its pleadings even after it already had finalized the protocols for its IH Trial and later OLE. *See* Appx10361-10410; Appx10411-10455.

Avadel, having litigated the entire case without giving notice that it would assert a safe harbor defense, cannot raise it now, particularly in light of the extreme prejudice that would result to Jazz. *See infra*, at 39-42; *In re Frescati*, 886 F.3d at 313 n.29 ("Affirmative defenses must be raised as early as practicable, not only to avoid prejudice, but also to promote judicial economy."); *Bradford-White Corp. v. Ernst & Whinney*, 872 F.2d 1153, 1161 (3d Cir. 1989) ("Obviously it would be grossly unfair to allow a plaintiff to go to the expense of trying a case only to be met by a new defense after trial."). Avadel's attempt to inject its new defense fails for at least this reason.

2. Avadel Unconditionally Stipulated To Infringement

Avadel's belated invocation of the safe harbor defense is barred for a separate reason—Avadel expressly and categorically disclaimed its safe harbor defense by stipulating to infringement without including an exemption for any alleged safe harbor activities that it planned.

"A stipulation of fact that is fairly entered into is controlling on the parties and the court is generally bound to enforce it." *Ring & Pinion Serv. Inc. v. ARB Corp.*, 743 F.3d 831, 836 (Fed. Cir. 2014) (holding "district court erred by failing to enforce the parties' stipulation"); *Stubbs v. Wyndham Nassau Resort*, 447 F.3d 1357, 1365 (11th Cir. 2006) ("A stipulation between parties, particularly in the litigation context when approved by the court is a binding contract enforceable on the basis of contract principles."); *Analytical Eng'g, Inc. v. Baldwin Filters, Inc.*, 425 F.3d 443, 453 (7th Cir. 2005) ("Stipulations by parties are nothing more than a contract. . . . [A party] is bound by that contract and all the legal ramifications of that contract."); *Branch Banking & Trust Co. v. D.M.S.I., LLC*, 871 F.3d 751, 765 n.4 (9th Cir. 2017) ("Parties are bound by their stipulations."); *Gander v. Livoti*, 250 F.3d 606, 609 (8th Cir. 2001) ("Valid stipulations are controlling and conclusive, and courts must enforce them.").

Infringement is a question of fact that the jury would have decided absent Avadel's stipulation. *See Natera*, 106 F.4th at 1375. Yet Avadel made the strategic decision to concede infringement—without qualification—prior to trial and gambled on a jury verdict of invalidity.

Appx4311-4313. Avadel cannot now invoke a non-infringement safe harbor argument as a workaround to bypass an unfavorable jury verdict.

Nor can Avadel disguise its waived safe harbor argument as a challenge to the "scope of [the district court's] authority to grant injunctive relief," (Br. 26)—an assertion that presupposes that each use is non-infringing under the safe harbor. Allowing Avadel to do so would effectively usurp the factfinder's role in determining the factual question of whether the safe harbor exception applies to each infringing act.

Avadel next argues (Br. 27-28) that it had no basis to raise the safe harbor before trial because "Jazz never accused Avadel of infringement through an IH clinical trial, nor could it have done so at or before trial, since Avadel launched its inaugural IH clinical trial only recently." But Jazz need not identify in its complaint every way in which Avadel possibly could "make, use, or offer for sale" an infringing product—Jazz sought to enjoin *all* such future conduct. Appx10008; Appx10169. And Avadel's stipulation, which acknowledges its product infringes Jazz's patent, is not limited either temporally or by type of activity. Certainly Avadel would have known when it entered the stipulation in February 2024 whether it had a basis to assert the safe harbor defense it now

raises: Avadel (1) publicly disclosed that it planned to seek an IH indication for Lumryz as early as June 2023, (Appx11591); (2) finalized its IH Trial and OLE protocols in January 2024, the month before the stipulation, (ECF 23, Stern Decl. Ex. 2); and (3) its CEO Greg Divis confirmed at trial that Avadel was seeking an IH indication (Appx9263, 519:17-19).

Nor can Avadel succeed on its argument that, at the permanent injunction argument, Jazz "disclaimed any intention of seeking injunctive relief as to such clinical trials." Br. 28-29. By that point in time, Avadel had notice that Jazz sought to enjoin any study not currently ongoing. Appx4550. Jazz's narrow exemption for currently ongoing studies did not encompass *future* studies. In any event, as the district court clarified in its order denying Avadel's motion for a stay pending appeal, any studies currently ongoing when the district court issued the injunction are not enjoined. Appx40-41. Jazz is not challenging that determination on appeal.

For this additional reason, Avadel cannot now invoke the safe harbor defense.

3. Avadel Waived Any Safe Harbor Defense By Failing To Raise It In The Injunction Briefing

Separately, this Court should find Avadel's safe harbor argument waived because Jazz's permanent injunction request sought to enjoin Avadel's IH activities but Avadel omitted from its briefing opposing that motion any argument that the safe harbor protects its IH activities.

This Court "does not 'review' that which was not presented to the district court." *Sage Prods., Inc. v. Devon Indus., Inc.*, 126 F.3d 1420, 1426 (Fed. Cir. 1997) ("[T]his court declines to consider . . . novel infringement arguments" on appeal.); *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1044 (Fed. Cir. 2016) ("We limit our appellate review to the evidence of record before the district court."); *Rotec Indus., Inc. v. Mitsubishi Corp.*, 215 F.3d 1246, 1257 n.4 (Fed. Cir. 2000) ("[W]e must review the district court's order in light of what is present in the record, regardless of what might have been presented."). Courts have even found waiver where a defense was properly pled, but "[defendant] simply did not attempt to establish [its] affirmative defense before or at trial." *Bradford-White*, 872 F.2d at 1161.

Jazz's proposed injunction order expressly detailed the conduct it sought to enjoin. Appx4550. Jazz explicitly requested that "Avadel may

not seek approval from the U.S. Food and Drug Administration for any indication that was not already part of Lumryz's approved product labeling as of March 4, 2024." Appx4550. IH is one such indication. Jazz also excluded making, using, and selling Lumryz for "*currently-ongoing* clinical trials and studies"—and did not carve out any future clinical trials and studies from its request.[3] Appx4550. In response, Avadel presented no evidence or argument that any of its activities allegedly fell under the safe harbor. Avadel's last-ditch effort to raise the safe harbor at the injunction hearing does not remedy this failure because counsel's unsworn statements are not evidence and cannot sustain a non-infringement finding. *Gemtron Corp. v. Saint-Gobain Corp.*, 572 F.3d 1371, 1380 (Fed. Cir. 2009) (noting "unsworn attorney argument . . . is not evidence"); *Galen Med. Assocs., Inc. v. United States*, 369 F.3d 1324, 1339 (Fed. Cir. 2004) (same).

Avadel now attempts (Br. 9-11, 15-17, 23-24) to shoehorn into the record on appeal evidence it neglected to present to the district court through the declarations of Jennifer Gudeman and Dr. Thomas Stern

[3] Even though Jazz sought to enjoin all future infringing conduct (Appx10008), Jazz carved specific conduct out of its injunction request in light of the public interest.

attached to Avadel's stay briefing. But, by then, the district court had issued its injunction after Avadel had the opportunity to include whatever evidence it wanted with its opposition to Jazz's injunction request. Indeed, in the district court, Avadel submitted declarations from an Avadel CEO Greg Divis and Dr. Stern, but neither discussed the issues raised by Ms. Gudeman or Dr. Stern in their stay brief declarations. Appx5972-5979; Appx5981-5992.

This belated attempt to raise the factual question of non-infringement on appeal—after failing to raise an affirmative defense and offering no evidence or briefing on non-infringement before appeal—should be rejected.

4. Resurrecting The Safe Harbor Defense Would Unduly Prejudice Jazz

Finally, and relatedly, Avadel may not invoke the safe harbor affirmative defense now because permitting it to do so would unduly prejudice Jazz.

"[T]he Third Circuit's law governing waiver is based on the possible prejudicial effect of raising affirmative defenses after the pleadings." *Stored Value Sol'ns, Inc. v. Card Activation Techs., Inc.*, 499 F. App'x 5, 13 (Fed. Cir. Dec. 10, 2012); *In re Frescati*, 886 F.3d at 313-14. "The

purpose of requiring the defendant to plead available affirmative defenses in his answer is to avoid surprise and undue prejudice by providing the plaintiff with notice and the opportunity to demonstrate why the affirmative defense should not succeed." *Robinson v. Johnson*, 313 F.3d 128, 134-35 (3d Cir. 2002); *see also Shell Oil Co. v. U.S.*, 896 F.3d 1299, 1315 (Fed. Cir. 2018) (affirming waiver and denial of leave to amend due to unfair prejudice where party had "ample opportunity to broaden the scope of the litigation . . . but chose not to do so in a timely fashion") (quotes omitted).

In *Bradford-White*, for instance, the defendant attempted after trial to revive a pleaded defense on which it "did not file a motion or present argument before the district court on the [defense] at any time before or at the trial." 872 F.2d at 1160. The Third Circuit held that "it would be grossly unfair to allow a plaintiff to go to the expense of trying a case only to be met by a new defense after trial." *Id.* at 1161.

Here, had Avadel properly pleaded and litigated the safe harbor defense (or even raised it in injunction briefing), Jazz would have pursued a different strategy below. For example, Jazz would have: (i) sought written and oral discovery concerning Avadel's purportedly

non-infringing activities and the alleged necessity of further clinical studies; (ii) included specific contentions regarding why Avadel's activities were not subject to the safe harbor; (iii) conducted expert discovery regarding the extent to which clinical studies would have been necessary to obtain approval of any non-narcolepsy indication; and (iv) presented evidence before the district court. Avadel stripped Jazz of those opportunities.

The prejudice to Jazz is clear. Discovery is needed to determine whether the safe harbor defense applies. *See, e.g.*, *Amgen*, 944 F.3d at 1340 (holding "[s]ubstantial evidence," including fact and expert testimony and documents, "support[ed] the jury's finding that the batches at issue were not manufactured 'solely for uses reasonably related to the development and submission of information' to the FDA"); *Ares-Serono, Inc. v. Organon Int'l B.V.*, 151 F.R.D. 215, 219 (D. Mass. 1993) (reasoning plaintiff needed access to documents to test assertions that activities were "reasonably related" under Section 271(e)(1) and that wrongly denying such access "would effectively endow defendants with the unilateral ability to decide the scope and the reach of section 271"). And yet, Avadel allowed discovery to progress, entered into a stipulation

of infringement, tried claims of invalidity to a jury, and briefed the injunction at the district court without reference to or evidence in support of a safe harbor defense. Such prejudice underscores why the Court must reject Avadel's safe harbor arguments.

B. The District Court Did Not Clearly Err In Rejecting Avadel's Safe Harbor Arguments

Even if Avadel could overcome its waiver of the safe harbor defense, the district court did not clearly err in declining to find the fact-specific defense applicable here, where Avadel presented no factual evidence showing that the safe harbor defense protects the enjoined conduct.

1. The Safe Harbor Inquiry Is A Factual, Rather Than Legal, Inquiry

This Court and the Supreme Court have repeatedly held that the application of the safe harbor's limited protection is a "factual issue" requiring the presentation of evidence. *See Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402, 406 (Fed. Cir. 1989); *see also Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 208 (2005) (declining to review for first time on appeal "sufficiency of the evidence" of jury's finding that safe harbor defense did not apply to defendant's clinical trials, where "evidence presented at trial ha[d] yet to be reviewed under the standards

set forth in the jury instruction"); *Amgen*, 944 F.3d at 1340 (reviewing "substantial evidence" supporting lack of safe harbor protection).

The defendant has the burden to prove by a preponderance of the evidence that the safe harbor applies. *Merck KGaA*, 545 U.S. at 200. This Court has never held otherwise. With no factual record upon which to rely, Avadel imagines that its enjoined activities "are non-infringing as a matter of express statutory law." Br. 22. Specifically, Avadel argues that conducting additional clinical trials for its new IH indication and seeking FDA approval are "expressly defined as non-infringing under the Section 271(e)(1) safe harbor." Br. 18. But Avadel cites no authority to support its position that the safe harbor functions as a statutory limit on the scope of activities subject to an injunction without *any* inquiry into the facts surrounding the activities in question. Indeed, Avadel's precedent-free argument flies in the face of decisions by this Court and the Supreme Court explaining that the applicability of the safe harbor rests upon the fact-finder's assessment of the evidence submitted in the district court. Avadel's interpretation of Section 271(e)(1)—which would allow infringers to unilaterally declare which activities do and do not infringe a patent, without any evidentiary process—is contrary to the law.

2. Avadel Has Not Shown That The Safe Harbor Protects The Enjoined Conduct

Nor can Avadel show the district court abused its discretion or clearly erred in declining to find the requirements of the safe harbor defense met. Avadel failed to put forward evidence that *each use* of the patented invention is "solely for uses reasonably related to the development and submission of information" to the FDA, such that the use is necessary for obtaining FDA approval, and failed to show that the infringing dosage form that Lumryz embodies meets the safe harbor's "patented invention" requirement because the FDA already has approved it.

a. Avadel Failed To Prove Its Use Of Jazz's Patented Invention Is "Solely For Uses Reasonably Related To The Development And Submission Of Information" To The FDA

To invoke the safe harbor, an infringer must prove that "each act of [infringement] was for uses reasonably related to submitting information to the FDA." *Edwards*, 96 F.4th at 1353. In other words, the infringer must show that its "otherwise infringing activities [are] *necessary* to obtain regulatory approval." *Eli Lilly*, 496 U.S. at 671 (emphasis added); *Edwards*, 96 F.4th at 1352 (safe harbor protects only activities "consistent with the collection of data *necessary* for filing an application

with the FDA") (emphasis added). "Each of the accused activities must be evaluated separately to determine whether the exemption applies." *Merck KGaA*, 545 U.S. at 200.

Avadel makes no such showing here.

First, Avadel presented no evidence to the district court in opposing Jazz's permanent injunction request sufficient to satisfy this requirement. What Avadel does identify in the record post-dates the district court's injunction ruling. Br. 9-11, 15-17, 23-24 (citing Stern and Gudeman declarations submitted with post-injunction stay briefing). Avadel cannot rely on evidence never presented for the district court's consideration before it issued the injunction. *See, e.g.*, *Sage*, 126 F.3d at 1426 (This Court "does not 'review' that which was not presented to the district court."); *Apple*, 839 F.3d at 1044 (same); *Rotec*, 215 F.3d at 1257 n.4 ("[W]e must review the district court's order in light of what is present in the record, regardless of what might have been presented.").

Second, while Avadel asserts (Br. 22) that the safe harbor "categorically protects clinical trials," the very cases Avadel cites contradict the bright-line rule that Avadel urges. Rather, Avadel must show that such clinical trials are "*necessary* to obtain regulatory

approval," *Eli Lilly*, 496 U.S. at 671 (cited at Br. 25, 36) (emphasis added). Avadel presented no evidence that each use of Lumryz in each future clinical trial, including its proposed OLE, meets this requirement. Nor could it.

No future clinical trial beyond the currently-ongoing IH Trial would be required to obtain approval for IH. Avadel concedes as much, stating that it intends to request FDA approval for an IH indication for Lumryz after it completes its currently-ongoing IH Trial. Br. 11.[4] And OLE studies are generally not required for FDA approval. Appx7646 (stating FDA's preference for blinded trials and recognizing potential for bias in open-label trials).

Avadel now makes conclusory arguments that OLEs are necessary for "recruiting" patients to Avadel's IH trial and "generating important long-term safety data." Br. 22-23. But, as the district court recognized, Avadel has not shown "that it would be unable to recruit participants to

[4] Nor has Avadel presented evidence that its currently-ongoing IH Trial is necessary to obtain FDA approval for an IH indication. Avadel has requested, and been granted approval for, a new indication for the treatment of pediatric narcolepsy without conducting *any* clinical trials, instead relying on Jazz's clinical trials in pediatric narcolepsy. Appx7624-7629; Appx7630-7635.

the [IH] study without open-label extensions." Appx43. Nor has Avadel shown that the "long-term safety data" it seeks is necessary to obtain FDA approval. Avadel's new declarations do not demonstrate any clear error in the district court's finding in this regard. Rather, Avadel's conduct in commercially marketing Lumryz for the treatment of narcolepsy, and the long-term safety data generated from real-world use of Lumryz, undermine Avadel's argument. And Avadel correctly does not take the position that safety data generated in narcolepsy would be inapplicable to IH—it would. Taking Avadel's position to its extreme, every use forever would generate "long-term safety data," so Avadel could never be enjoined from using or selling the infringing drug. That cannot be. Even assuming Avadel had presented substantial evidence to prove that additional clinical trials are protected by the safe harbor (it did not), it could not do so for OLE for the reasons stated above.

Third, Avadel has not proved based on the evidence presented to the district court that its IH activities are *solely* for uses reasonably related to the development and submission of information to the FDA. *Amgen*, 944 F.3d at 1340 (substantial evidence supported jury finding that certain batches of drug product were not "'solely for uses reasonably

related to the development and submission of information' to the FDA"); *see also Eli Lilly*, 496 U.S. at 678 (noting protections of safe harbor "imposed" "only for the purpose of obtaining premarketing approval"); *Edwards*, 96 F.4th at 1358 (Lourie, J., dissenting) ("The word 'solely' was included in the statute to ensure that infringing activity that was performed for purposes other than the development and submission of information under a federal law regulating drugs would not be exempt."); *Biogen, Inc. v. Schering AG*, 954 F. Supp. 391, 396-97 (D. Mass. 1996) (concluding large scale production and market preparation took defendant out of "safe harbor").[5]

Finally, even if the enjoined uses do not need to be *solely for* FDA approval, Avadel has the burden to show that each use in each trial of the infringing dosage form is *not solely* related to commercial activity. *Edwards*, 96 F.4th at 1354-55. This analysis requires a use-by-use analysis presented to the trier of fact in the first instance. *Merck KGaA*, 545 U.S. at 200. But Avadel presented no evidence proving that the

[5] *See* Petition for a Writ of Certiorari, *Edwards*, No. 24-428 (U.S. Oct. 11, 2024) (petitioning the U.S. Supreme Court to answer: "Whether, under Hatch-Waxman's safe harbor, an infringing act is '*solely* for uses reasonably related' to the federal regulatory process, when the infringing act is performed for both regulatory and non-regulatory uses").

enjoined studies would not be solely for commercial purposes. And, had Avadel even raised the safe harbor, Jazz would have presented evidence to rebut any such argument. For instance, Jazz would have presented evidence from experts in the field on the amount of clinical studies (or patients in studies) necessary to support an additional indication, given that "open-label studies are merely dressing up marketing exercises as research." Appx43 (internal quotes omitted). The record below reinforces that additional clinical studies and the OLE would be solely for commercial purposes given the evidence of Avadel exaggerating its clinical data to push its place in the market ahead of Jazz, including Avadel's history of: (1) negotiating with PBMs to COMMERCIALLY SENSITIVE INFORMATION [redacted] (Appx6); (2) publicizing clinical trial results in press releases, publications, and at investor and scientific conferences before FDA approval for an indication (*see* Appx7651-7653; Appx7654-7665; Appx7666-7675); and (3) widely publicizing its activities with respect to IH specifically, including communicating with prescribing doctors about the IH Trial (*see* Appx7676-7712; Appx7713-7733; ECF 7, Ex. G, ¶¶ 7-9).

Avadel's reliance (Br. 31) on *Telectronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992), does not require a contrary conclusion. *Telectronics* did not involve an adjudicated infringer already commercially marketing the infringing product and the case instead merely confirms the general principle that disseminating data otherwise necessary for obtaining FDA approval of a product in the first place does not remove the protections of the safe harbor. *Id.* at 1524. And there, as in all safe harbor cases, the alleged infringer actually presented evidence to the district court to support its arguments that its uses were not solely for commercial purposes but rather were "reasonably related to FDA approval." *Id.* at 1523. Here, Avadel has not. Rather Avadel admits (Br. 31) that it intends to publicize the results of its clinical trials to investors, physicians, and patients while the infringing product is commercially available. Thus, even accepting Avadel's improper new evidence, Avadel cannot prove its activities are not solely for a commercial purpose.

b. The Lumryz Dosage Form Does Not Meet The Safe Harbor's "Patented Invention" Requirement

The safe harbor also does not apply to Avadel's use of Lumryz because Avadel has not shown the Lumryz dosage form falls under the

safe harbor's "patented invention" requirement, as opposed to being a research tool used in the FDA approval process.

This Court has never held that an adjudicated infringer can invoke the safe harbor to expand the use of an infringing product that is already commercially marketed.

This Court has held that, to qualify as a "patented invention" under Section 271(e)(1) and benefit from safe harbor protection, the infringing product must "*itself [be] subject to the FDA premarket approval process*," and not just "used in the development of FDA regulatory submissions." *Proveris Sci. Corp. v. Innovasystems, Inc.*, 536 F.3d 1256, 1265 (Fed. Cir. 2008) (emphasis added); *see also Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1071 (Fed. Cir. 2011) ("Every decision examining the statute has appreciated that § 271(e)(1) is directed to *premarketing* approval of generic counterparts before patent expiration.") (emphasis added); *Regenxbio*, 2022 WL 609141, at *3 (collecting cases holding "that where the patented product is not subject to FDA premarket approval, the safe harbor does not apply"). In this regard, "[t]he legislative history makes clear that the exemption 'does not permit the commercial sale of a patented drug by the party using the drug to develop [federal

regulatory] information." *Edwards*, 96 F.4th at 1358 (Lourie, J., dissenting) (quoting H.R. Rep. No. 98-857, pt. 1, at 45).

Here, Lumryz embodies the patented dosage form, has FDA approval, and is being commercially marketed. Lumryz is no longer subject to the "premarket approval process," and the safe harbor cannot protect Avadel's unpermitted use of Jazz's patented invention to expand its commercial presence and infringement.

Avadel's only arguments for why the "patented invention" requirement is supposedly met is because "Lumryz is not a piece of lab equipment," and it needs FDA approval for a new IH indication. Br. 30. But such arguments are not responsive to Jazz's point, which is that the patented invention in this case is the Lumryz dosage form—which the FDA already has approved.

Avadel is simply using Lumryz, an FDA approved product, as a tool in an attempt to expand its labeling to include IH as a new indication. "In short, [Avadel] is not a party seeking FDA approval for a *product* in order to enter the market to compete with patentee[]. Because the [infringing Lumryz dosage form] is not subject to FDA premarket approval, and therefore faces no regulatory barriers to market entry upon

patent expiration," the safe harbor defense does not apply. *Proveris*, 536 F.3d at 1265. And Jazz's patented invention receives no improper patent term extension because Avadel can begin using Lumryz as a research tool to support studies, just as in *Proveris*, upon patent expiration. The patented invention at issue in this case therefore cannot be subject to the safe harbor exception.

C. Avadel's Remaining, Newly-Raised Non-Infringement Arguments Fail

Finally, neither of Avadel's other new non-infringement arguments demonstrate the district court abused its discretion.

1. The Patent Act Does Not Protect The Enjoined Conduct

Avadel is wrong to contend that "the Patent Act also makes clear that seeking FDA approval in and of itself is not infringing activity," Br. 24, because Section 271(a) of the Patent Act explicitly deems infringing "uses" of the patented invention. 35 U.S.C. § 271(a). Here, Avadel is "us[ing]" Jazz's patented invention to seek FDA approval in violation of Section 271(a), as Avadel well knows given its citation (Br. 24-25) to the safe harbor immediately after claiming non-infringement under Section 271(a). But the safe harbor states only that Avadel can use a patented invention for the "development and submission" of

information and is silent on seeking FDA approval. In the context of infringement cases brought under Section 271(e)(2), FDA approval cannot take place if infringement is proven. *See* 35 U.S.C. § 271(e)(4)(A). Avadel provides no reason, let alone legal support, for this Court to conclude that enjoining the FDA from approving an application under 35 U.S.C. § 271(e)(4)(A) for infringement under Section 271(e)(2) is permissible, but enjoining a Section 271(a)-adjudicated-infringer under 35 U.S.C. § 283 from asking the FDA for that very same approval is wrong.

2. The First Amendment Does Not Protect The Enjoined Conduct

Likewise meritless is Avadel's invocation (Br. 25) of the First Amendment as justification for its infringement.[6]

"The first amendment is not a license to trammel on legally recognized rights in intellectual property." *Dallas Cowboys Cheerleaders, Inc. v. Scoreboard Posters, Inc.*, 600 F.2d 1184, 1187-88 (5th Cir. 1979) (affirming preliminary injunction and observing that

[6] While Avadel faults (Br. 16) the district court for never addressing Avadel's First Amendment argument, Avadel never presented this argument to the district court. *See* Appx5652-5677.

"[p]reliminary injunctions are a common judicial response to the imminent infringement of an apparently valid copyright"); *see also Cable/Home Commc'n Corp. v. Network Prods., Inc.*, 902 F.2d 829, 849 (11th Cir. 1990) ("[T]he district court's injunction was targeted specifically at the infringing activity and, therefore, did not infringe on any First Amendment interests of the defendant."). Indeed, courts routinely affirm injunctions prohibiting infringement of intellectual property rights, which are "not [cases] of government censorship, but a private plaintiff's attempt to protect its property rights." *Dallas Cowboys Cheerleaders, Inc. v. Pussycat Cinema, Ltd.*, 604 F.2d 200, 206 (2d Cir. 1979) ("The propriety of a preliminary injunction where such relief is sought is so clear that courts have often issued an injunction without even mentioning the first amendment.").

For example, in *Eli Lilly & Co. v. Medtronic, Inc.*, the district court held a patent infringer in contempt for violating its injunction. 735 F. Supp. 652, 662 (E.D. Pa. 1990), *vacated on other grounds*, 915 F.2d 670 (Fed. Cir. 1990). The infringer argued that "the First Amendment permits the dissemination of 'scientific and educational information' … unless there is a vital government interest to the contrary." *Id.* The

district court rejected that defense and explained that "[t]he vital government interest is the protection of the patent from acts that threaten its sanctity." *Id.* To protect that "vital government interest," "[r]easonable restraints may be placed on an infringer to both eliminate the consequences of past bad acts and to prevent further encroachment on the patent." *Id.* Accordingly, the district court concluded that "[t]he First Amendment cannot save [the infringer] from contempt." *Id.*

Here, the district court's order does not enjoin seeking FDA approval in a vacuum: it is narrowly "targeted specifically at the infringing activity" to protect Jazz's patented invention from further infringement. *Cable/Home Commc'n Corp.,* 902 F.2d at 849. Unsurprisingly, none of the cases Avadel cites address the First Amendment in the context of patent infringement or enjoining infringing conduct. Rather, the law—and commonsense—dictate that Avadel is simply wrong to contend the First Amendment provides Avadel "a license to trammel," *Dallas Cowboys Cheerleaders, Inc.*, 600 F.2d at 1188, on Jazz's patent rights despite the "vital government interest" in "the protection of the patent from acts that threaten its sanctity," *Eli Lilly,* 735 F. Supp. at 662.

3. In Any Event, The District Court Would Not Have Abused Its Discretion By Enjoining Non-Infringing Conduct As Necessary To Prevent Infringement

Even if Avadel had preserved these new non-infringement arguments (it did not) and even if these arguments had merit (they do not), the district court still did not abuse its discretion because non-infringing conduct may be narrowly enjoined as necessary to prevent infringing conduct.

This Court has "never barred" "judicial restraint of non-infringing activities" and "instead ha[s] repeatedly stated that district courts are in the best position to fashion an injunction tailored to prevent or remedy infringement." *TiVo Inc. v. EchoStar Corp.*, 646 F.3d 869, 890 n.9 (Fed. Cir. 2011) (en banc).

Here, the district court was well within its discretion to narrowly enjoin Avadel from seeking FDA approval, conducting additional clinical trials, and conducting an OLE because doing so was necessary to prevent Avadel from expanding its infringement of Jazz's patent by marketing Lumryz for non-narcolepsy indications, including IH.

First, enjoining Avadel from seeking FDA approval is necessary to prevent Avadel from marketing Lumryz for IH because requesting FDA

approval for IH would unavoidably result in marketing Lumryz for IH—rendering the injunction meaningless.

To request IH approval for Lumryz, Avadel must submit proposed labeling that includes an IH indication and information regarding the results of Avadel's IH Trial. *See* 21 C.F.R. § 201.56(c), § 201.57(c)(2), § 201.57(c)(15), § 314.70(b)(2)-(3); 21 U.S.C. § 355(b)(1)(A)(vi). If the FDA approves Avadel's request for IH (the FDA cannot be enjoined here), the updated Lumryz label with the IH indication would be distributed to patients and prescribers, 21 C.F.R. § 201.100(d), and included with certain marketing materials. U.S. Food and Drug Administration, *Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs,* Draft Guidance for Industry (August 2015) (available at https://www.fda.gov/media/70768/download) ("Generally, the requirements in 21 C.F.R. 201.100(d) have been fulfilled by including the full FDA-approved package insert (PI) with promotional labeling materials.").

Inclusion of a non-narcolepsy indication (*e.g.*, IH) on the Lumryz label constitutes marketing because, as this Court repeatedly has held, a

label with language "instructing how to engage in an infringing use[] show[s] an affirmative intent that the product be used to infringe." *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320, 1333-34 (Fed. Cir. 2021); *see also Braintree Labs. v. Breckenridge Pharm.*, 688 F. App'x 905, 910 (Fed. Cir. May 5, 2017) (Because the label "instructs how to engage in an infringing use, it shows an affirmative intent that the product be used to infringe."). The inclusion of IH on Lumryz's label would demonstrate Avadel's intent for physicians to prescribe and patients to use—and Avadel to profit from selling—Lumryz for IH. Allowing Avadel to seek FDA approval as to IH thus would render the injunction meaningless as to the sale and marketing for IH—activities Avadel concedes are infringing.

Beyond the Lumryz label, Avadel has admitted—even in briefing before this Court (Br. 31-32)—that it would issue press releases disclosing the IH approval, inform investors of the approval, inform patients and physicians of the approval, and use the approval in negotiations with PBMs. These are all quintessential marketing activities the injunction prohibits since Lumryz is already commercially available.

In addition, if Avadel received approval for IH and continued its current negotiating strategy, PBMs could [redacted], and patients taking Xywav for IH would be [redacted] to [redacted]. Avadel already has made off-label sales of Lumryz for IH before the injunction, and allowing Avadel to seek FDA approval would provide it more avenues to do so.

Second, enjoining Avadel from conducting additional clinical trials, including the OLE, is also necessary to prevent Avadel from marketing Lumryz for IH. Avadel concedes (Br. 31-32) that it plans to disseminate the clinical trial data it obtains from additional clinical trials. Not only is Avadel differently situated than the alleged infringer in *Telectronics*, *see supra*, at 50, but Avadel has presented no evidence that the data generated was "reasonably related to FDA approval" or would not be solely for commercial purposes, *Edwards*, 96 F.4th at 1354-55. Given the evidence before it, and even if deemed non-infringing, the district court did not abuse it discretion in enjoining additional clinical trials or seeking FDA approval as necessary to prevent Avadel from expanding its in infringing conduct.

II. AVADEL FAILS TO SHOW ANY ABUSE OF DISCRETION AS TO THE *eBAY* FACTORS

Avadel also fails to show that the district court abused its discretion in issuing a permanent injunction based on its factual findings as to each of the *eBay* factors.[7]

District courts routinely grant permanent injunctions against adjudicated infringers. 35 U.S.C. § 283; *see, e.g.*, *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 861-64 (Fed. Cir. 2010), *aff'd*, 564 U.S. 91 (2011) (affirming entry of permanent injunction notwithstanding infringer's irreparable injury, balance of hardships, and public interest arguments). The *eBay* factors require: "(1) that [plaintiff] has suffered an irreparable injury; (2) that remedies available at law, such as monetary damages, are inadequate to compensate for that injury; (3) that, considering the balance of hardships between the plaintiff and defendant, a remedy in equity is warranted; and (4) that the public interest would not be disserved by a permanent injunction." *eBay Inc. v.*

[7] Avadel errs in arguing (Br. 33 n.9) that the district court made a "late-breaking decision to enjoin" the OLE and thus did not consider the *eBay* factors. As this Court recognized, the district court's stay order was not an "expansion" of the injunction, but rather a "clarifi[cation]." ECF 30 at 3.

MercExchange, L.L.C., 547 U.S. 388, 391 (2006). "[D]istrict courts are in the best position to fashion an injunction tailored to prevent or remedy infringement." *Broadcom Corp. v. Emulex Corp.*, 732 F.3d 1325, 1339 (Fed. Cir. 2013); *see also Apple*, 809 F.3d at 646 (same).

A. The District Court Did Not Abuse Its Discretion In Concluding That Irreparable Harm And The Lack Of An Adequate Remedy At Law Favored An Injunction

Avadel cannot show the district court abused its discretion in deciding that Avadel's entrance into the IH market with an infringing product would irreparably harm Jazz and leave Jazz with no adequate remedy at law.

As this Court has explained, "[w]here two companies are in competition against one another, the patentee suffers the harm—*often irreparable*—of being forced to compete against products that incorporate and infringe its own patented inventions." *Douglas Dynamics, LLC v. Buyers Prods. Co.*, 717 F.3d 1336, 1345 (Fed. Cir. 2013) (emphasis added); *see also Bio-Rad Lab'ys, Inc. v. 10X Genomics Inc.*, 967 F.3d 1353, 1378 (Fed. Cir. 2020) (finding irreparable harm where "first mover advantage" is lost). That irreparable harm, and the corresponding "need to protect [market] exclusivity," is "certainly [] at its highest when the infringer is

one's fiercest competitor." *Apple*, 809 F.3d at 642 (holding patentee established irreparable harm).

Here, the district court enjoined the same irreparable harm under circumstances remarkably similar to those affirmed by this Court. The district court concluded that "Lumryz's entrance into the market for IH would irreversibly harm Jazz's market share and damage its ability to build its reputation as the exclusive market leader." Appx24. The district court reasoned that "with [Lumryz's] FDA approval," Jazz "will compete head-to-head" with what would be its fiercest (and only) competitor against its own patented invention "in a newly-developing [IH] market." Appx24. This determination was wholly consistent with this Court's teaching—and a far cry from an abuse of discretion.

Avadel does not—because it cannot—contest the district court's findings and instead argues (Br. 33-35) that Jazz never linked its assertion of irreparable harm specifically to the "development and submission of an application for FDA approval of a new IH indication for Lumryz." But, as discussed *supra*, at 37-42, Avadel neither raised this argument in the district court nor presented evidence to support it. Avadel cannot raise this argument for the first time on appeal. *See*

Fresenius USA, Inc. v. Baxter Int'l, Inc., 582 F.3d 1288, 1296 (Fed. Cir. 2009) (making a specific challenge below "does not preserve all possible challenges to that finding"); *In re Nickelodeon Consumer Privacy Litig.*, 827 F.3d 262, 276 n.81 (3d Cir. 2016) ("This court has consistently held that it will not consider issues that are raised for the first time on appeal.").

Even if preserved, the "flexible" causal nexus requirement is satisfied through "some connection" between the alleged harm and the infringing acts. *Apple, Inc. v. Samsung Elecs. Co.*, 735 F.3d 1352, 1364 (Fed. Cir. 2013). This Court has acknowledged that nexus and affirmed injunctions prohibiting non-ongoing clinical trials to prevent future harm. *See, e.g.*, *Natera*, 106 F.4th at 1381-83 (affirming injunction barring future, non-ongoing clinical trials).

Here, a clear and direct connection exists between Avadel seeking FDA approval and the harm redressed by the injunction. Seeking FDA approval would necessarily result in marketing Lumryz for IH. *See supra*, at 57-60. Avadel itself admitted in its emergency stay motion that the district court's injunction "will disrupt Avadel's efforts to secure FDA approval and its *opportunity to promptly market Lumryz* for IH upon

FDA approval." ECF No. 7 at 3 (emphasis added). Avadel itself has confirmed its causal nexus argument lacks merit.

Avadel also errs in arguing (Br. 35) "the threat of any harm to Jazz from the marketing of Lumryz to IH patients is (at this point) entirely hypothetical and speculative" because Avadel has not yet obtained "FDA approval to market Lumryz to IH patients." But the whole "purpose of an injunction is to prevent *future*" harm. *United States v. W.T. Grant Co.*, 345 U.S. 629, 633 (1953) (emphasis added); *see also AMG Cap. Mgmt., LLC v. Fed. Trade Comm'n*, 593 U.S. 67, 75 (2021) ("injunction typically offers prospective relief against ongoing or future harm" (citation omitted)). FDA approval is not a prerequisite for an injunction. And the cases that Avadel cites (Br. 35) have nothing to do with patent infringement injunctions.

Here, Avadel has expressly conceded that its objective is to "promptly market Lumryz for IH upon FDA approval." ECF No. 7 at 3. Indeed, Avadel has already begun the activity it calls "entirely hypothetical and speculative"—marketing Lumryz for IH. Avadel has publicly conceded as much by acknowledging that its "primary goal" is to "switch[]" Jazz patients to Lumryz. *See, e.g.*, Appx9013. As the district

court found, Avadel's interest in the IH market is based largely on Jazz having the only FDA-approved treatment and, consequently, that "a lot of opportunity remained" because Jazz is in the early stages of growing the market. Appx24-25. For these reasons, Avadel's arguments do not undermine—much less show clear error in—the district court's correct finding that "Jazz established that it suffered some irreparable harm through past loss of market share and price erosion" as a result of Lumryz being on the market for the treatment of narcolepsy. Appx5-10. And, as a legal matter, "[p]ast harm to a patentee's market share, revenues, and brand recognition is relevant for determining whether the patentee 'has suffered an irreparable injury.'" *i4i Ltd. P'ship*, 598 F.3d at 861 (quoting *eBay*, 547 U.S. at 391) (emphasis omitted); *see also id.* at 862 ("Although injunctions are tools for prospective relief designed to alleviate future harm, by its terms the first *eBay* factor looks, in part, at what has already occurred."); *TEK Glob., S.R.L. v. Sealant Sys. Int'l, Inc.*, 920 F.3d 777, 793 (Fed. Cir. 2019) ("Head-to-head competition and lost market share tend to evidence irreparable harm."). For these reasons, the district court did not abuse its discretion in finding that irreparable harm and the lack of an adequate remedy at a law favored an injunction.

B. The District Court Did Not Abuse Its Discretion In Ruling That The Balance Of Hardships Favored An Injunction

Avadel also fails to show that the district court abused its discretion in deciding that the "balance of the equities also tips in Jazz's favor" (Appx27)—indeed, Avadel does not contest the factual findings underlying that conclusion.

This Court repeatedly has held that "requiring a patentee to 'compete against its own patented invention . . . places a substantial hardship' on the patentee" and "strongly favors an injunction." *Apple*, 809 F.3d at 645, 647. "One who elects to build a business on a product found to infringe cannot be heard to complain if an injunction against continuing infringement destroys the business so elected." *Windsurfing Int'l, Inc. v. AMF, Inc.*, 782 F.2d 995, 1003 n.12 (Fed. Cir. 1986).

Here, the district court explained that "enjoining Lumryz for IH would not spell 'the end of Avadel.'" Appx27. Indeed, Avadel did not dispute below that it stands to make billions of dollars on infringing sales of Lumryz to treat narcolepsy, which the district court's injunction does not affect. *See* Appx4579-80; Appx6066; Appx7553. The district court relied on Avadel's representation that it "ha[d] not yet started any [IH]

clinical trials and would not do so if an injunction was granted." Appx27 (cleaned up). But Avadel decided to initiate its IH Trial anyway, and "cannot be heard to complain if an injunction against continuing infringement destroys the business so elected." *Windsurfing Int'l*, 782 F.2d at 1003 n.12. In contrast, requiring Jazz to compete against its own patented invention places substantial hardship on Jazz, particularly where Jazz is working to grow its position and reputation in the IH market as having the first and only FDA approved treatment for IH. Appx27.

Unable to contest these findings, Avadel once again raises a new argument on appeal. Avadel now argues (Br. 36) that, by "depriv[ing] Avadel of the chance to line up FDA approval in advance of the expiration of the '782 patent," the district court improperly "conferr[ed] an indirect extension of Jazz's patent term."

But, as the district court clarified, "[w]hile the Order enjoins Avadel from seeking FDA approval for IH, the Order does not enjoin Avadel from s*ubmitting information or results* from ongoing clinical studies to the FDA." Appx41. Thus, Avadel may "line up" such approval

and simply is enjoined from asking for FDA approval prior to patent expiration.

And Avadel's argument (Br. 36-37) that the district court should have declined to issue an injunction based on the history of the litigation neither raises a legal error nor identifies any clearly wrong factual finding. Instead, Avadel seeks to improperly color this Court's perception of Jazz, urging this Court to favor the interests of Avadel as the adjudicated infringer over the protection to which Jazz, as the innovator, is entitled. Nothing about Avadel's argument changes the fact that allowing Avadel to enter the IH market would require Jazz to "compete against its own patented invention," *Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1156 (Fed. Cir. 2011), and provides no basis to vacate or modify the injunction.

C. The District Court Did Not Abuse Its Discretion In Concluding That The Public Interest Favored An Injunction

Finally, Avadel cannot show that the district court abused its discretion in deciding that public interest considerations favor enjoining Lumryz as to the IH market. Appx27-31.

While "the public often benefits from healthy competition," it "does not benefit when that competition comes at the expense of a patentee's investment-backed property right." *Apple*, 809 F.3d at 647. That is because "the encouragement of investment-based risk . . . is the fundamental purpose of the patent grant, and is based directly on the right to exclude." *Id.* at 646-47. "In evaluating whether the public interest favors the grant of an injunction, the district court should focus on whether a critical public interest would be injured by the grant of injunctive relief." *Natera*, 106 F.4th at 1380 (internal quotes and cite omitted).

Avadel is wrong to argue (Br. 37) that the district court improperly placed the "burden" on Avadel as to the public interest factor. The district court determined that Jazz had established the public interest in "incentivizing 'innovative drug companies to continue costly development efforts,'" (Appx31 (quoting *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368, 1383 (Fed. Cir. 2006))), and that Avadel had failed to show that the alleged benefits of Lumryz for IH patients outweighed this significant public interest in view of the evidence Jazz presented regarding Xywav's use once-nightly to treat IH. The "court did not, as [Avadel] asserts, shift

the burden to [Avadel]; rather, the court found that [Jazz] made 'a prima facie showing,'" *Acumed LLC v. Stryker Corp.*, 551 F.3d 1323, 1331 (Fed. Cir. 2008), of a public interest in incentivizing innovation and that Xywav is already used once-nightly in IH. The "weight given to particular evidence falls well within the discretion of the court" and it was within the district court's "discretion to conclude that the public interest was not disserved by an injunction." *Id.*

As the district court correctly recognized, Jazz's Xywav product is a safe and effective treatment for the once-nightly treatment of IH, and "Avadel has not shown that Lumryz offers any other distinct benefits to patients with IH." Appx30. Thus, "Avadel failed to show that Lumryz is a superior or unique treatment for IH" and "Avadel's claim that '[p]hysicians have [] urged Avadel to seek FDA approval for Lumryz in IH' is similarly insufficient to outweigh the public's interest in enforcing patent rights and encouraging innovation." Appx31.

While Avadel argues (Br. 38) that the district court erred by "draw[ing] its own conclusions about clinical superiority" because "[i]t is the FDA's responsibility to evaluate the efficacy and superiority of new drugs," Avadel ignores that the district court—not the FDA—makes

findings of fact in issuing an injunction as a remedy for adjudicated infringement. *Astrazeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1061 (Fed. Cir. 2010) ("[T]he FDA is not the arbiter of patent infringement issues."). Nor is the district court under any obligation to wait for the FDA to make a finding. *Sys. Fuels, Inc. v. United States*, 818 F.3d 1302, 1307 (Fed. Cir. 2016) ("Cases are decided on the facts of record, not a set of facts that may come into being in the future."). And Avadel's assertion (Br. 38) of a "manifest public interest in the clinical investigation and expert administrative review that goes into the FDA approval process" simply seeks to elevate the rights of an infringer over the rights of an innovator, whom the law seeks to protect.

In arguing (Br. 38-39) that the "district court is ill-equipped to weigh for itself the relative public benefit or detriment of Lumryz's availability" and that "[i]t is not possible to weigh the public benefit" without FDA input, Avadel seems to suggest that the district court give Avadel *carte blanche* to infringe and suspend entering final judgment until the FDA issues a decision on Avadel's purported Orphan Drug applications. Not only would that likely take years, but it disregards that weighing the evidence to reach a conclusion on injunctive relief, even

where FDA approval is outstanding, is a "role [that] belongs exclusively to the district court." *Acumed LLC v. Stryker Corp.*, 483 F.3d at 811; *see also GlaxoSmithKline*, 7 F.4th at 1332 (noting FDA's position that "it has no expertise in patent law and that a court is the appropriate forum for determining the scope of patent rights").

For these reasons, the district court did not abuse its discretion in finding that the public interest favors an injunction.

CONCLUSION

This Court should affirm the district court's permanent injunction.

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitations of Federal Circuit Rule 32(b)(1) because it contains 13,999 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2).

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CERTIFICATE OF COMPLIANCE WITH RULE 25.1(e)(2)

This motion complies with the limitations set forth in Federal Circuit Rule 25.1(d)(1)(A) and contains 15 unique words (including numbers and images) marked as confidential.

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I hereby certify that on November 7, 2024, I electronically filed the foregoing using the Court's CM/ECF system, which will send notifications to all counsel registered to receive electronic notices.

I further certify that I caused the confidential version of the foregoing document to be served via electronic mail to all counsel of record, at the addresses below:

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